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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,808	12/07/2001	H. William Bosch	029318-0799	8203

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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,808	BOSCH ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-76 and 93-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-76 and 93-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 14-38, 51-76, 93-104 and 107-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. US 5,565,188, in view of Pace et al. US 6,177,103.

Wong teaches a composition containing nanoparticles comprising a therapeutic agent, and a surface modifier adsorbed to the surface of the nanoparticles (see abstract; and column 1, lines 51-67). Therapeutic agent is in a discrete crystalline phase, and can include a wide variety of drug including naproxen (column 3, lines 67 through column 4, lines 1-67; and column 5, line 9). Wong also teaches therapeutic agent having particle size of less than about 100 μm, or particles can be reduced to average particle size of less then 400 nm (column 5, lines 50-59; column 6, lines 7-9;

and column 10, lines 1-15). Therapeutic is dispersed in at least one liquid medium, such as water or safflower oil (column 4, lines 4-19). Surface modifier can be present in an amount of 0.1-90% (column 13, lines 25-31). The composition further comprises other excipients, and can be incorporated into dosage form suitable for rectal, vaginal, and topical administration including dry powder formulation (column 12, lines 48-64; and column 14, lines 5-13). Wong further teaches the use of additional surface modifier (column 9, lines 17-19).

Wong does not expressly teach cationic surface modifier.

Pace teaches a submicron particle comprising water-insoluble drugs, and combination of surface modifiers (column 4, lines 46-62). Surface modifiers include benzalkonium chloride and cetyltrimethylammonium bromide (column 6, lines 34-61). Thus, it would have been obvious to one of ordinary skill in the art to modify the nanoparticles composition of Wong using the surface modifiers in view of the teaching of Pace to obtain the claimed invention, because Pace teaches using surface modifiers to stabilize the generated small particles and suppress any tendency of particle agglomeration or particle growth while they are formed (column 5, lines 46-51), because Pace teaches the use of cationic surfactants suitable for poorly soluble therapeutic compound (columns 5-6), because Pace teaches the use of similar therapeutic compound used by Wong, and because Wong teaches the use of surface modifier having rehological properties that produced a nanoparticles composition useful as bioadhesive and/or control release agents for the delivery of therapeutic agents (column 3, lines 30-49).

It is noted that Wong is silent as to the teaching that the therapeutic is liquid at room temperature. However, it is the position of the examiner that the therapeutic taught by Wong would be liquid at room temperature, because Wong teaches the use of the same active agent, *e.g.*, naproxen. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claims 39-50, 105 and 106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. US 5,565,188, in view of Mantelle et al. US 6,316,022 and Wik US 5,938,017.

Wong is relied upon for the reasons stated above. Wong does not teach water-soluble active agent.

Mantelle teaches a transdermal composition comprising low molecular weight drug that is liquid at room temperature including pesticides, sunscreen and cosmetic agent (column 4, lines 34-58). Mantelle also teaches water-soluble active agent such as nicotine (column 5, lines 12-18; see also Wik at column 7, line 60 (for the teaching that nicotine is water-soluble)). The composition further comprises enhancers (surface modifier), and co-solvents such as mineral oil, or alcohol (column 5, lines 66 through column 6, lines 1-39). Thus, it would have been obvious to one of ordinary skill in the art to modify the nanoparticles of Wong for the active agents in view of the teaching of Mantelle, because Wong teaches a nanoparticles composition suitable for a variety of

therapeutic agents, and because Mantelle teaches water-soluble therapeutic active agent can be prepared for topical administration.

Claims 39-50, 105 and 106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wong et al. US 5,565,188, in view of Pace et al. and Mantelle et al. US 6,316,022 and Wik US 5,938,017.

Wong in view of Pace are relied upon for the reasons stated above. The references do not teach water-soluble active agent.

Mantelle teaches a transdermal composition comprising low molecular weight drug that is liquid at room temperature including pesticides, sunscreen and cosmetic agent (column 4, lines 34-58). Mantelle also teaches water-soluble active agent such as nicotine (column 5, lines 12-18; see also Wik at column 7, line 60 (for the teaching that nicotine is water-soluble)). The composition further comprises enhancers (surface modifier), and co-solvents such as mineral oil, or alcohol (column 5, lines 66 through column 6, lines 1-39). Thus, it would have been obvious to one of ordinary skill in the art to modify the nanoparticles of Wong for the active agents in view of the teaching of Mantelle, because Wong teaches a nanoparticles composition suitable for a variety of therapeutic agents, and because Mantelle teaches water-soluble therapeutic active agent can be prepared for topical administration.

Response to Arguments

Applicant's arguments filed 07/28/06 have been fully considered but they are not persuasive.

Applicant argues that Wong does not teach cationic surface stabilizer, and therefore, does not anticipate the claimed invention. However, in response to applicant's argument, it is noted that Wong besides teaching the surface stabilizer, further teaches the use of cationic surfactant, such as dodecyltrimethyl ammonium (column 11, lines 10-16).

Applicant argues that the cationic surfactant taught by Wong is used as cloud point modifiers, not surface modifiers. However, while applicant is entitle to his or her own lexicographer, it is noted that Wong teaches the use of cationic surfactant in the nanoparticle composition to obtain a nanoparticle composition for the same use as the claimed invention, namely, a bioadhesive nanoparticulate composition (column 3, lines 45-49). Wong teaches using cationic surfactant to influence the cloud point of surface modifiers so that the surface modifiers do not dissociate from the surface of the nanoparticles, therefore, nanoparticles do not agglomerate and retain their effective average particles size (column 10, lines 31-41). Accordingly, Wong teaches using cationic surfactant to stabilize the surface modifier so that the surface modifiers stay on the surface of the nanoparticle. In another word, cationic surfactant is used as a surface stabilizer. Furthermore, Wong is cited in view of Pace for the teaching of using cationic surfactant to increase the stability of the small particle formation. Thus, one of ordinary skill in the art would have been motivated to combine the teachings of Wong

and Pace to obtain the claimed invention, because both Wong and Pace teach the use of the same cationic surfactant in a nanoparticle composition. The modification is the use of cationic surfactant in addition to the surface modifier taught by Wong. The transitional phrase "comprising of" in the present claims do not preclude the nonionic surface modifier taught by Wong. This is further evident by the dependent claims of the present claimed invention. See for example claims 101, 103, 105, 107 and 109. The claims require the additional of non-cationic surfactant.

Applicant argues that there is no motivation to combine Wong and Pace, because Pace does not teach the use of cationic surfactants in the making of bioadhesive nanoparticulate composition. In response to applicant's argument, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Pace is relied upon for the teaching of cationic surfactants in stable submicron particle composition. Pace teaches the submicron particle composition useful for a wide variety of water-insoluble drugs, which is useful in pharmaceutical art. Thus, one of ordinary skill in the art would look into Pace to modify Wong, because Wong teaches nanoparticle useful for water-insoluble drugs as well. The bioadhesive properties of the submicron particles in Pace is obvious, since Pace teaches the use of the claimed cationic surface modifiers. When the prior art teaches the identical chemical structure,

the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Applicant argues that Mantelle does not cure the deficiencies of Wong because it does not teach cationic surface stabilizers. In response to applicant's argument, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Mantelle is relied upon solely for the teaching of the specific water-soluble drugs that can be used in a transdermal composition.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. Tran
Patent Examiner
Art Unit 1615